THE INHERENT CONFORMATIONAL PREFERENCES OF GLUTAMINE-CONTAINING PEPTIDES: THE ROLE FOR SIDE-CHAIN BACKBONE HYDROGEN BONDS

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Glutamine is widely known to be found in critical regions of peptides which readily fold into amyloid fibrils, the structures commonly associated with Alzheimer's disease and glutamine repeat diseases such as Huntington's disease. Building on previous single-conformation data on Gln-containing peptides containing an aromatic cap on the N-terminus (Z-Gln-OH and Z-Gln-NHMe), we present here single-conformation UV and IR spectra of Ac-Gln-NHBn and Ac-Ala-Gln-NHBn, with its C-terminal benzyl cap. These results point towards side-chain to backbone hydrogen bonds dominating the structures observed in the cold, isolated environment of a molecular beam. We have identified and assigned three main conformers for Ac-Gln-NHBn all involving primary side-chain to backbone interactions. Ac-Ala-Gln-NHBn extends the peptide chain by one amino acid, but affords an improvement in the conformational flexibility. Despite this increase in the flexibility, only a single conformation is observed in the gas-phase: a structure which makes use of both side-chain-to-backbone and backbone-to-backbone hydrogen bonds.